REMARKS

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the amendments and remarks made herewith, which place the application in condition for allowance.

I. Status of the Claims and Formal Matters

Claims 1-17 are pending in this application. Claims 1-15 are currently amended and Claims 18-32 are new.

These amendments have been made simply for clarification and to place the claims in condition for allowance. No new matter has been added by these amendments. Support for the amendments can be found throughout the specification. The amendments presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

The Examiner has made a number of objections to informalities. Specifically, the specification allegedly did not contain a Brief Description of the Drawings as required by 37 C.F.R. §1.74. The specification has been amended and is in compliance with 37 C.F.R. §1.74.

Additionally, the specification contained disclosure relating to "shaded amino acids" and "black-rimmed box" referred to in Figure 3, on page 12, lines 16-19. Figure 3 allegedly did not show these items. The specification has been amended to remove the disclosure relating to these items.

The term "GIuC" was referred to on page 13, line 5. The Examiner contends that "GIuC" is not known. The specification has now been amended to read "GluC".

Further, Figure 7 contained a legend that shows a cross-hatched box for "ester-cleaving enzyme" and a black box for "Pseudomonas sp. lipase". Figure 7 shows cross-hatched bars and clear bars, but no black bars. Amended Figure 7, submitted herewith, now shows a cross-hatched box and a clear box in the legend that now corresponds to the bar graph.

In view of the amendments to the specification, reconsideration and withdrawal of the objections to the application are therefore respectfully requested.

II. Sequence Listing

The Examiner has required the submission of sequence disclosures in compliance with 37 C.F.R. §1.821 through §1.825 regarding the amino acid sequences in Figure 3. The sequences described as "Q59798" and "Q56008" in Figure 3 are now SEQ ID No. 2 and SEQ ID No. 3, respectively. The sequence described as "EGS-Enzym" corresponds to SEQ ID No. 1. The amendments to the specification, which now include a Brief Description of the Drawings, now refers to these sequences by their sequence identifiers.

Further to the Sequence Listing filed March 17, 2004, enclosed is a corrected copy of the Sequence Listing in both paper and computer readable form. Applicants respectfully request entry of the enclosed Sequence Listing.

It is respectfully asserted that the sequence disclosure contained in the application now fully complies with the requirements set forth in 37 C.F.R. § 1.821 to § 1.825. Accordingly, reconsideration of Applicants failure to comply with the sequence listing rules is respectfully requested.

It is respectfully submitted that the Sequence Listing conforms to the requirements of 37 C.F.R. §1.823(b). The Statements required by 37 C.F.R §1.821(f) and (g) are set forth below.

Pursuant to 37 C.F.R. §1.821 (g), the undersigned hereby states that this submission, filed in accordance with 37 C.F.R. §1.821 (g), does not contain new matter.

Pursuant to 37 C.F.R. §1.821 (f), the undersigned hereby states that the content of the paper and computer readable copies of the Sequence Listing submitted in accordance with 37 C.F.R. §1.821 (c) and (e), respectively, are the same.

In view of the amendments, remarks and enclosures herewith, the application complies with the requirements of the 37 C.F.R. §1.821-1.825 relating to nucleotide and/or amino acid sequences.

III. Rejections under 35 U.S.C. §101

Claims 1-5 and 13-15 were rejected under 35 U.S.C. §101 for allegedly being directed to non-statutory subject matter. The amendments to claims 1-5 now recite, "An isolated ester-group-cleaving enzyme...". Claims 13-15 were drawn to use claims, which is not proper in U.S. Patent practice. The amendments to claims 13-15 are now expressed as method claims with

distinct steps. Therefore, reconsideration and withdrawal of the rejections under 35 U.S.C. §101 are respectfully requested.

IV. Rejections under 35 U.S.C. §112, second paragraph

Claims 1, 2-5, 7-8 and 10-13 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner alleges that claims 1, 2 and 12 are incorrect in the recitation of the bacterial species, which should be italicized. In response, the bacterial species of claims 1, 2 and 12 have been italicized, thereby obviating the rejection.

The Examiner alleges that claim 1 is indefinite in the recitation of "optionally". In response, claim 1 has been clarified to delete the recitation of "optionally", thereby obviating the rejection.

The Examiner alleges that claim 3 is indefinite in the recitation of "optionally", "especially" and "and/or". In response, claim 3 has been clarified to delete the recitation of "optionally", "especially" and "and/or", thereby obviating the rejection.

The Examiner alleges that claim 4 is indefinite in the recitation of the 4 parentheses. In response, claim 4 has been clarified to delete the parentheses, thereby obviating the rejection.

The Examiner alleges that claim 5 is indefinite and confusing in the recitation of "resulting from . . . insertion . . . of amino acids of SEQ ID NO:1". In response, claim 5 has been clarified to recite the substitution of amino acids of SEQ ID NO:1, insertion of amino acids into SEQ ID NO:1 or deletion of amino acids from SEQ ID NO:1, thereby obviating the rejection.

The Examiner alleges that claims 7 and 8 are indefinite in the recitation of "or against a synthetic peptide or protein". In response, claims 7 and 8 have been clarified to delete that recitation, thereby obviating the rejection.

The Examiner alleges that claim 10 is indefinite in the recitation of "and/or" and "optionally". In response, claim 10 has been clarified to delete the recitation of "and/or" and "optionally", thereby obviating the rejection.

The Examiner alleges that claim 11 is indefinite in the recitation of "especially". In response, claim 11 has been clarified to delete the recitation of "especially", thereby obviating the rejection.

The Examiner alleges that claim 13 is indefinite in the recitation of "and/or". In response, claim 13 has been clarified to delete the recitation of "and/or", thereby obviating the rejection.

It is believed that the rejections under 35 U.S.C. § 112, second paragraph have been overcome. Reconsideration and removal of the rejections are respectfully requested.

V. Rejections under 35 U.S.C. §112, first paragraph

Claims 7-9 and 16-17 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner alleges that the specification does not teach that an antibody was made against the enzyme of claim 1 or a synthetic peptide or protein or a hybridoma cell producing the monoclonal antibody and therefore the specification does not meet the requirements of the written description requirement or enable one of ordinary skill in the art to make these items. Applicants respectfully disagree and traverse the rejection.

The specification states that methods for production of antibodies and hybridomas are routine, and provides a reference that teaches suitable methods (see, e.g., page 6, first paragraph of the specification as filed). It is accepted in the art that antibody production is a routine procedure, as highlighted by fact that most researchers now have antibodies made on a contract basis by one of the many contract antibody production companies that exist. All that one has to do is send a sample of the purified protein, and/or the nucleic acid that encodes that protein, to such a company for production of the desired antibodies. Thus, one of skill in the art would not need any additional instructions, other than those provided in the specification, in order to make the claimed antibodies, or indeed have them made by others. Applicants also respectfully direct the Examiner to U.S. Patent No. 4,558,005 (a copy of which is enclosed herewith) as evidence that methods for the production of a hybridoma cell line and the antibodies derived therefrom are well known to one of skill in the art. The Examiner is respectfully requested to consider and

make of record the herewith submitted patent, which is also cited on the accompanying Information Disclosure Statement and PTO-1449.

The Examiner alleges that the specification does not teach that a genetically modified microorganism was ever made containing the gene encoding the enzyme of claim 1 and therefore, the specification does not meet the requirements of written description as to claims 16-17. The Examiner also alleges that claims 16-17 constitute new matter. Applicants respectfully disagree and traverse the rejection.

First, it was within the knowledge and skill of one of ordinary skill in the art in the relevant field to deduce a nucleotide sequence from the amino acid sequence of SEQ ID NO. 1 and to provide a genetically modified microorganism containing the encoded claimed protein. As evidence, Applicants submit concurrently herewith an article by Knoerzer et al. entitled "Expression of synthetic genes encoding bovine and human basic fibroblast growth factors (bFGFs) in *Escherichia coli*"; Gene 75 (1989) pp. 21-30 (hereinafter "Knoerzer"). The Examiner is respectfully requested to consider and make of record the herewith submitted article, which is also cited on the accompanying Information Disclosure Statement and PTO-1449.

For example, on page 24, right column, item a and Figure 1 on page 25 of Knoerzer, a synthetic gene encoding 146 amino acids of bovine bFGF was designed on the basis of the known amino acid sequence. Therefore, the skilled artisan is capable of constructing an expression strain starting from the known amino acid sequence by synthesizing oligonucleotides and assembling them to the gene of interest in the form of synthetic DNA. Furthermore, as shown in Figure 3, lane d on page 27 of Knoerzer, the protein of interest can be expressed in an organism of interest. The skilled artisan merely has to transfer the teaching of Knoerzer to the present invention to obtain a clone expressing the desired protein.

Second, it is another question to which extent the synthetic gene reflects the natural nucleotide sequence which encodes the protein of interest in the genome. However, because of the degeneration of the genetic code, the synthetic codons must be chosen to be amino acid conservative and further according to the three statements mentioned on page 24, right column, item (a) of Knoerzer.

Third, the subject matter of claims 16-17 do not constitute new matter. The Examiner is respectfully directed to page 4, paragraph 3 which recites that "both natural and genetically modified microorganisms are suitable" (emphasis added). Furthermore, one of ordinary skill in

the art would have been motivated to construct the claimed genetically modified organisms without undue experimentation given the teachings of the specification and coupled with what was known in the art, as evidenced by Knoerzer.

Claims 5-6 and 13-15 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner alleges that the specification does not teach one of ordinary skill in the art how to produce a mutant of SEQ ID NO:1 having enzymatic activity. The Examiner also contends that the specification does not teach one of ordinary skill in the art to use any synthetic peptide or protein or any ester-group-cleaving composition to degrade an ester-group-containing compounds. Applicants respectfully disagree and traverse the rejection.

Applicants respectfully submit that the regions of the claimed protein required for ester group cleaving activity were well known to one of skill in the art and submit concurrently herewith an article by Perez et al., titled "Cloning, characterization, and expression in *Streptomyces lividans* 66 of an extracellular lipase-encoding gene from *Streptomyces* sp. M11" in Gene 123 (1993):109-114. The Examiner is respectfully requested to consider and make of record the herewith submitted article, which is also cited on the accompanying Information Disclosure Statement and PTO-1449.

The conserved region of the active site of the claimed protein is shown in Figure 3 on page 112 of Perez. Therefore, the regions of the claimed protein required for ester group cleaving activity were known to one of ordinary skill in the art. Applicants submit that given the teachings of Perez and the specification, one of ordinary skill in the art would be able to produce a mutant of SEQ ID NO:1 having enzymatic activity. Directed mutagenesis in a specific region of a protein (e.g., the conserved region of the active site) and testing the resultant mutant for enzymatic activity is routine experimentation for one of ordinary skill in the art.

Furthermore, one of ordinary skill in the art is able to make and use a synthetic peptide or protein or any ester-group-cleaving composition to degrade an ester-group-containing compounds given the teachings of the specification and Perez. A combination of the teachings of the specification (e.g., SEQ ID NO. 1) and Perez (e.g., the conserved region required for ester group cleaving activity) provides one of ordinary skill in the art to make a synthetic peptide or protein or any ester-group-cleaving composition and to test the peptide or protein or any ester-composition for ester-group-cleaving activity.

It is believed that the rejections under 35 U.S.C. § 112, first paragraph have been overcome. Reconsideration and removal of the rejections are respectfully requested.

VI. Rejections under 35 U.S.C. §102(b), §102(e), and §103(a)

Claims 1-6 and 10-15 were rejected under 35 U.S.C. §102(b)/(e) as anticipated by, or in the alternative, under 35 U.S.C. §103(a) as obvious in view of Kellis et al (U.S. Patent No. 6,254,645; hereinafter "Kellis"), Hollick ((1982) Microbio 35: 187-196; "Hollick"), Kleeberg et al ((1998) Appl. Environ. Microbiol. 64(5): 1731-1735; "Kleeberg"), or Fett et al ((1993) J. Appl. Microbiol. 86: 561-568; "Fett").

Kellis allegedly teaches that polyesterases may be isolated from *Thermomonospora* species. Hollick allegedly teaches that *Thermomonospora fusca* produces an esterase, an esterase-lipase, and a lipase. Kleeberg allegedly teaches that *Thermomonospora fusca* produces an enzyme that degrades aliphatic-aromatic copolymers. Fett allegedly teaches that *Thermomonospora fusca* produces an enzyme that hydrolyzes cutin, a molecule containing ester bonds. The Examiner asserts that these references relate to the instantly claimed enzyme, and further states that confirmation of the identity of the enzyme would require testing of these enzymes by the Applicants. The Examiner further alleges that it would have been obvious to isolate and purify the *Thermomonospora* enzymes of the present invention.

Kellis discloses *Thermomonospora* strains in column 6, line 67, but does not specifically teach *Thermomonospora* enzymes useful in cleaving polyesters (see column 12, Table I). All of the tested enzymes show activity for diethylterephthalate (DET), a low molecular weight water-soluble ester. However, only one enzyme out of the 51 disclosed non-*Thermomonospora* enzymes in the Table I shows activity for polyethylene terephthalate (PET), specifically cutinase from *Pseudomonas mendocina*. This demonstrates that the mechanisms of ester cleavage of water-soluble esters and of polyesters are different, which suggests that there is enzyme specificity for these substrates. The provisions of Kellis disclose that only one enzyme of the 51 enzymes tested displays activity against polyesters, which suggests that this activity may be rare. Therefore, Kellis does not anticipate or render the instant invention obvious, since Kellis has failed to adequately define the specific activities of *Thermomonospora* enzymes.

Hollick describes purported enzymatic activities of, *inter alia*, *Thermomonospora fusca*. As disclosed on page 188 of Hollick, assays of enzymatic activities were performed using whole

organisms and double dialysis antigen preparations with "API ZYM strips". Notably, Hollick does not isolate individual enzymes comprising these activities. Hollick discloses the activities of "esterase C4" and "esterase-lipase C8" in the table provided on page 190, but fails to describe an enzyme or enzymatic activity that can cleave ester groups at the interface of polyester solid substrates. Further, the enzymatic activities taught by Hollick are not related to those of the present invention. The activities reported by Hollick are constitutive, i.e., always present. The present invention relates to, *inter alia*, an inducible isolated enzyme, as reflected in the amended claims and in the Declaration of Dr. Rolf-Joachim Mueller presented herewith. Therefore, Hollick does not anticipate or render the present invention obvious.

Kleeberg describes a culture of *Thermomonospora fusca* cells obtained from a spore suspension (see page 1734, left column, line 18). Kleeberg discloses polyesters such as BTA 40:60 (1,4-butanediol/terephthalic acid/adipic acid) that are subjected to whole cells. Kleeberg does not use a cell-free supernatant containing the enzyme, nor does Kleeberg isolate a particular enzyme comprising this activity.

The Examiner is respectfully directed to Figure 2 of Kleeberg, which concerns the degradation of BTA 40:60 by a specific culture of *T. fusca*, namely *T. fusca* K13g. Figure 2 shows that the activity of K13g does not result in weight loss and degradation of BTA 40:60 in one 24-hour period. In fact, weight loss and degradation is only observed after a 1-day lag phase, followed by constant weight loss over a period of 3 days. After approximately 32 hours, the weight loss was measured at 0.5 mg/cm^2. This is in contrast with Example 4 and Figure 4 of the instant application, which demonstrates that the claimed isolated enzyme contributes to weight loss of BTA 40:60 measured at 0.5 mg/cm^2 after only 17 hours. Clearly, this shows that the isolated enzyme activity is superior to the activity disclosed in Kleeberg. It is respectfully submitted that at the time the instant application was filed, the specific activity attributed to a specific, isolated enzyme had not been identified. Therefore, Kleeberg does not teach or disclose the enzyme of the present invention, and further, does not anticipate or render the present invention obvious.

Turning back to the cited art, Fett describes inducible cutinase activity in culture supernatants of *Thermomonospora* species. Individual cutinase enzymes were not isolated or purified. The instant invention relates to isolated *T. fusca* enzymes that have physical properties that are different from the cutinase described in Fett. Firstly, the cutinase of Fett has an optimum

pH of 11 (see Fett abstract). The instant invention describes enzymes whose optimum pH is between 6 and 7 (page 5 of the specification). Secondly, the cutinase described in Fett has an optimum temperature of below 50°C, while the instant invention describes an enzyme that has an optimum temperature of 65°C, well above 50°C. Therefore, Fett does not teach or suggest the enzymes of the present invention. Further, Fett does not anticipate or render the present invention obvious.

Claims 1-15 were rejected under 35 U.S.C. §103(a) for allegedly being unpatentable over Kellis, Hollick, Kleeberg, or Fett in view of Goldwasser et al (U.S. Patent No. 4,558,005; "Goldwasser"). Goldwasser allegedly teaches how to produce polyclonal and monoclonal antibodies and hybridomas from a protein. The Examiner contends that it would have been obvious to one of ordinary skill in the art to obtain the enzyme taught by the cited at and to use this protein to produce antibodies according to Goldwasser.

As discussed above, the enzymes of the present invention are not taught or suggested by Kellis, Hollick, Kleeberg, or Fett. Therefore, antibodies directed to these proteins are novel and not obvious, regardless of the teachings of Goldwasser. Further, the Examiner's rejection under §103(a) contradicts the rejection under 35 U.S.C. §112, first paragraph. The Examiner has asserted that the specification failed to enable antibody production, because "there is some inventive contribution to making an antibody" (page 5, second paragraph of the June 2, 2004 Office Action). Either the production of an antibody is a routine matter, and can readily be performed by the skilled artisan who is in possession of the purified protein – in which case, the rejection under §112 would be improper – or having possession of a purified protein alone does not render the production of the antibody obvious, because antibody production is itself an inventive process – in which case, the rejection under §103 would be improper.

Therefore, in view of the foregoing, reconsideration and withdrawal of the rejections under §103(a) are respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, it is believed that the claims in this application are patentable, and early and favorable consideration thereof is earnestly solicited.

Respectfully submitted,

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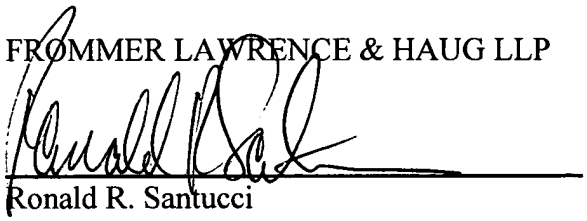
By: 

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